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EXAMINER	
TURNER, SHARON L	

ART UNIT	PAPER NUMBER
1647	37

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/322,289	Applicant(s) SCHENK, DALE B.	
	Examiner Sharon L. Turner	Art Unit 1647	

-- The MAILING DATE of this communication app ars on the cov r sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-8,10-58 and 60-81* is/are pending in the application.

4a) Of the above claim(s) *25-28,33,34,38-58 and 60-81* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8,10-24,29-32 and 35-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,2,4-8,10-58 and 60-81* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 August 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) **Other* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: IDS submissions Paper No's: 20, 27, 31-36.

Response to Amendment

1. The amendments filed 5-17-02, 7-30-02 and 8-13-02 have been entered into the record and have been fully considered.

2. Claims 56-81 are newly added. Claims 3, 9 and 59 are canceled. Claims 1-2, 4-8, 10-58 and 60-81 are pending.

3. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

4. As a result of Applicant's amendment, all rejections not reiterated herein have been withdrawn by the Examiner.

Claim Objections

5. Claim 5 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 5 depends from claim 1 and recites the further limitation, wherein the patient is asymptomatic. However, claim 1 requires that the patient be recognized and characterized as having amyloid deposits. Thus, the dependent claim is indefinite, see below, and/or non-limiting as amyloid deposits are clearly a symptom of amyloid disease. Even to the extent that claim 1 is directed to prevention, the claim requires that the disease and patient already be recognized and characterized as having amyloid deposits. Thus, claim 5 does not apparently further limit the patient population, but alternatively appears to broaden it. Clarification and/or correction is required.

Drawings

6. The drawing of Figure 11 is objected to because Figure 11 lacks an appropriate legend. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Rejections Maintained

Election/Restriction

7. Applicant's election with traverse of Group I, claims 1-24, 29-32 and 35-37, species A drawn to Abeta in Paper No. 14 is acknowledged. The traversal is on the ground(s) that the species are nonmutually exclusive. This is not found persuasive because while antibody cross-reactivity is well known, the specific antibodies recited for example in claims 25-28 may be generated via different peptide structures which results in alternative immunoreactivity, i.e., the recognition of distinct epitopes. Thus, while some antibodies may cross react, the antibodies as recited in the nonelected claims are different and are capable of different use, i.e., they are patentably distinct. Accordingly the species are in fact mutually exclusive and capable of separable use. It is also true that a search of antibodies to a single recited epitope would not necessarily reveal antibodies reactive to an alternative epitope, and thus the searches are not co-inclusive even to the generic recitation as recited in the claims, i.e., an antibody which binds Abeta may or may not recognize the recited epitope. For these reasons, the requirement is still deemed proper and is therefore made FINAL.

Applicants argue in the response of 5-17-02 that claims 35-37 are part of Group

I. Applicant's further argue that the Abeta epitopes are species within the Abeta genus and are not mutually exclusive.

Applicant's arguments filed 5-17-02 have been fully considered. Claims 35-37 were properly directed to the invention of Group I and were inadvertently omitted by the Examiner. Applicant's arguments in traverse of the species election requirement have been fully considered but are not persuasive. As set forth in MPEP 806.04(f), the general test as to when claims are restricted, respectively, to different species is the fact that one claim recites limitations which under the disclosure are found in a first species but not in a second, while a second claim recites limitations disclosed only for the second species and not the first. This is frequently expressed by saying that claims to be restricted to different species must recite the mutually exclusive characteristics of such species.

In instant case particular species are recited in a first species and not in a second species while the second species recites limitations disclosed only for the second species and not the first. For example, claim 25 is directed to residues 1-5 while claim 41 is directed to residues 13-28. Moreover, as particular "species" are in fact defined genera or subgenera, restriction for examination purposes is proper in that the search of the multiple genera and subgenera bear undue burden upon the Examiner for search and examination in a single case. Further, it is noted that the genera and subgenera are defined by separate characteristics as claimed and thus may be mutually exclusive and non-coextensive. It is not true that an antibody that binds within residues 1-5 for example, would necessarily bind any other peptide epitope of Abeta such as residues 1-

10, 1-16 or otherwise. As set forth previously, rejoinder amongst the generic, sub-generic and/or species claims would only be considered upon the indication of an allowable generic claim that properly linked the claimed inventions sharing the same characteristics. Applicants have designated Abeta as the elected invention. As no claim is indicated allowable, this point is deemed moot with respect to any rejoinder and accordingly the restriction/species election requirement is maintained.

8. Claims 25-28, 33-34 and 38-55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 14.

9. Newly submitted claims 56-58 and 60-81 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The claims recite patentably distinct methods that differ in reagents, steps, outcomes and effects. The searches are non-coextensive and a reference against any one element would not necessarily be relevant to any other.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 56-58 and 60-81 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim R jections - 35 USC § 102 or 103

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

11. Claims 1-2, 4-8, 10-21, 24, 29-32 and 35-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Nettleship et al., EP 613007, Aug. 31, 1994.

Nettleship et al., teach antibodies useful in the diagnosis and treatment of mammals suffering from Alzheimer's Disease, see in particular column 7, line 39-column 8, line 18. The antibodies are beta-amyloid peptides, particularly in beta-sheet conformation, but also include antibodies to alternative fragments, see in particular column 1, line 52-column 2, line 56. It is understood that the functional embodiment which characterizes the diagnostic and therapeutic relationship as disclosed in Nettleship hinges on the binding of the antibodies to the beta-amyloid peptides, see in particular reference in paragraph spanning columns 7-8 and reference to numerous assay systems suitable to detect agents which bind, column 8, lines 6-15. In addition, the compositions are pharmaceutical compositions which include formulations for parenteral administration (other than by intestinal, i.e., subcutaneous, intravenous, etc., as understood by the skilled artisan), see in particular column 8, lines 19-42. Thus, the

reference appears to be enabling for the determination of appropriate doses and routes of administration suitable for such binding to occur. Nettleship et al., teach the use of alternatively produced Abeta antibodies including to peptides which have adopted a random coil or alpha-helix conformation and to antibodies which are genetically engineered, antibody fragments, chimeric antibodies, recombinantly produced antibodies, and "humanized or murinized" antibodies as generated by replacement of CDR regions, see in particular column 5, lines 42-column 6, line 20. Thus the reference teaches the variable antibodies of claims 1 and 9-21. It is noted that the polyclonal sera would inherently include multiple antibodies and Ig isotypes. It is further noted that the patient population includes mammals and thus would encompass humans of various risk factors, symptoms and ages as recited in claims 2-8. Thus, the reference teachings anticipate the claimed invention.

Applicants argue at pp. 12-18 of the 5-17-02 response that the Nettleship reference fails to teach each and every limitation of the claims and that the reference is non-enabling for methods of prevention or treatment of Alzheimer's. Applicants additionally argue that the abandonment of the application in different jurisdictions evidences a lack of possession of the invention by Nettleship. As to particular claims, claim 5 is said to be patentable in that Nettleship does not teach treatment to patients other than those already having Alzheimer's disease. Claims 29-30 are argued to be patentable in that the antibodies of Nettleship are not of human origin.

Applicant's arguments filed 5-17-02 have been fully considered but are not persuasive. In contrast to Applicant's reading, the Examiner finds no evidence that Nettleship is directed solely to the use of particular antibodies. In contrast the reference as a whole evidences multiple assay procedures for binding amyloid and broadly teaches the use of all antibodies of the invention as useful in the diagnosis and

treatment of mammals suffering from Alzheimer's, see in particular column 8 and also columns 5-7. Just because Nettleship further elaborates as to particular embodiments, assays and/or "best mode" of effecting the invention, does not negate the reference's broad teachings. Nettleship is not required to make and test every embodiment any more than is Applicant. Nevertheless, particular limitations are no more critical to enablement of Nettleship than they are critical to Applicant's claims. Thus, as to those limitations that appear absent Applicant's claims as well as Nettleship's disclosure, are not deemed critical.

As to Applicant's new functional limitation, "wherein the administering of the antibody reduces levels of Abeta in the brains of the patient," the functional recitation is deemed to be met and/or inherent in all procedures where the teachings are the same as to antibody activity and administration. In particular all that is required of the administration of the antibody is that it specifically bind to Abeta peptide. The Nettleship reference teaches administration of Abeta antibodies effective in the treatment of Alzheimer's disease. Thus, any amount, route of administration, etc., effective for the treatment of Alzheimer's would be provided or enabled by the reference so long as the antibody specifically binds to Abeta.

Claim 5 is directed to patients that are asymptomatic. However, claim 1 from which claim 5 depends, stipulates that the patient is characterized as one having amyloid deposits and thus the patient would necessarily be recognized as one suitable for treatment as stipulated via Nettleship. Thus, the reference appears enabling for treatment of asymptomatic patients. Claims 10 and 29-30 are directed to human antibodies. Nettleship teaches making and using human antibodies at for example, column 6, lines 10-21 and lines 31-40. Claim 35-37 are directed to general administration procedures of antibodies including monitoring levels in patients,

administration for at least six months and in sustained release compositions. Nettleship et al., teach the administration of antibodies in pharmaceutical preparations and the compositions are effective in the treatment of Alzheimer's disease. Thus, as disclosed in particular at column 8, lines16-42 the Nettleship reference is enabling for antibody administration within the skill in the art including based upon monitoring levels within the blood of a patient, for a period of at least six months and in sustained release compositons. Thus, the reference teachings anticipate the claimed invention.

12. Claims 1, 9, 13, 15, 20 and 22-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Friedland et al., Mol. Neurobiol., 9(1-3):107-113, 1994.

Friedland et al., teach in vivo administration to mice of murine monoclonal antibody 10H3 which recognizes beta amyloid at the dosage of 10 ug to a mouse. This quantity correlates to at least 10 mg/kg body weight based on an average mouse weight of 10 g. Fab fragments were labeled with 99mTc for visualization and biodistribution was studied, see in particular Figures 1-2. Thus, the reference teachings anticipate the claimed invention.

Applicant's argue 5-17-02 that the Friedland reference is only directed to post-mortem brain and that thus the administration for imaging purposes cannot be considered to be in a patient.

Applicant's arguments have been fully considered but are not persuasive. While the purpose of Friedland was for imaging purposes Friedland teach administration in vivo and bio-distribution studies in mice in vivo of the monoclonal antibody specific to Abeta. Thus, the reference teachings can be deemed inherent.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-2, 4-8, 10-24, 29-32 and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nettleship et al., EP 613007, Aug. 31, 1994.

Nettleship et al., teach antibodies useful in the diagnosis and treatment of mammals suffering from Alzheimer's Disease, see in particular column 7, line 39-column 8, line 18. The antibodies are beta-amyloid peptides, particularly in beta-sheet conformation, but also include antibodies to alternative fragments, see in particular column 1, line 52-column 2, line 56. It is understood that the functional embodiment which characterizes the diagnostic and therapeutic relationship as disclosed in Nettleship hinges on the binding of the antibodies to the beta-amyloid peptides, see in particular reference in paragraph spanning columns 7-8 and reference to numerous

assay systems suitable to detect agents which bind, column 8, lines 6-15. In addition, the compositions are pharmaceutical compositions which include formulations for parenteral administration (other than by intestinal, i.e., subcutaneous, intravenous, etc., as understood by the skilled artisan), see in particular column 8, lines 19-42. Thus, the reference appears to be enabling for the determination of appropriate doses and routes of administration suitable for such binding to occur. Such would thus render obvious to the skilled artisan the dosage recitations of claims 22-23. Nettleship et al., teach the use of alternatively produced Abeta antibodies including to peptides which have adopted a random coil or alpha-helix conformation and to antibodies which are genetically engineered, antibody fragments, chimeric antibodies, recombinantly produced antibodies, and "humanized or murinized" antibodies as generated by replacement of CDR regions, see in particular column 5, lines 42-column 6, line 20. Thus the reference teaches the variable antibodies of claims 1 and 9-21. It is noted that the polyclonal sera would inherently include multiple antibodies and Ig isotypes. It is further noted that the patient population includes mammals and thus would encompass humans of various risk factors, symptoms and ages as recited in claims 2-8.

Applicants argue in the response of 5-17-02 that no other teachings are provided to supplement the teachings of Nettleship and that the reference is non-enabling.

Applicant's arguments have been fully considered but are not persuasive. The rejection is maintained as set forth above. The Examiner is not required to supplement the reference teachings in that they are deemed enabling. Proof of unobvious difference falls to Applicant's as the PTO has insufficient resources for comparison.

15. Claims 1-2, 4 and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walker et al., J. Of Neuropath. & Exp. Neurol., 53(4):377-83, 1994(a).

Walker et al., 1994 (a) teach in vivo labeling of cerebral amyloid with monoclonal antibody 10D5 in nonhuman primates. The anitbody is murine and interacts selectively to beta amyloid. The antibody is IgG1 kappa light chain and whole antibody or Fab fragments were administered at a dosage of 25 mg/kg im.

Walker et al., does not specifically teach administration in humans. However, Walker suggests that the methodology would be useful and desirable in patients with Alzheimer's disease, see in particular Discussion pp. 381-382. Thus, it would have been prima facie obvious given the positive results in nonhuman primates to employ the methodology in humans for similar in vivo imaging. One of skill in the art would expect positive results as demonstrated in primates, the most similar physiological paradigm to humans.

Applicant's argue in the response of 5-17-02 that Walker is directed to in vivo imaging and thus that the reference cannot render the claimed treatment obvious as the reference does not necessarily result in the prevention or treatment of Alzheimer's.

Applicant's arguments have been fully considered but are not persuasive. Motivation for the same purpose is not required of the prior art reference. The antibody is administered in the proper manner and possesses the appropriate activity. The Examiner is not required to supplement the reference teachings in that they are deemed enabling. Proof of unobvious difference falls to Applicant's as the PTO has insufficient resources for comparison.

Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 112

16. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

17. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 5 depends from claim 1 and recites the further limitation, wherein the patient is asymptomatic. However, claim 1 requires that the patient be recognized and characterized as having amyloid deposits. Thus, the dependent claim is indefinite and/or non-limiting as amyloid deposits are clearly a symptom of amyloid diseases. Even to the extent that claim 1 is directed to prevention, the claim requires that the disease and patient already be recognized and characterized as having amyloid deposits. Thus, clarification of the metes and bounds of "asymptomatic" is required.

Status of Claims

18. No claims are allowed.

Conclusion

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
October 7, 2003

Gary L. Kunz

GARY KUNZ
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